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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BERCH, MARK L

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 01/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/927,322

Examiner

Mark L. Berch

Applicant(s)

IMBACH ET AL.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12,14 and 17-21 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-12,14 and 17-21 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: .

Art Unit: 1624

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 12, 14, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO97/16452.

See Example 107. This corresponds to R5 = Hydroxyethyl (which is a substituted aliphatic hydrocarbon), q = 1, R1 = choice δ, in which R9 = methoxy, substituted by phenyl (note last word on page 72).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 5 rejected under 35 U.S.C. 103(a) as being unpatentable over WO97/16452.

Note above rejection. Claim 5 has R5 = Hydroxycycloalkyl rather than R5 = Hydroxyethyl of species 107. However, such a variant is taught as preferred by the reference, see for example page 14, line 9, and examples appear, e.g. example 65, 69, etc. Hence, this is an obvious variation.

Art Unit: 1624

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO97/16452.

Note anticipation rejection. R1 as COOH is listed as a preferred choice at page 20, line 9, and hence would be obvious.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 14, 17-21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- ✓ 1. The term, "for use" in claim 12 simply states an intention, which is a mental step, not a patentable limitation. Hence the claim is improperly dependent on claim 1, as it does not further limit the claim on which it depends. Alternatively, this may be intended as a method of use claim, in which case, the claim is garbled, as it begins as a compound claim, and ends as a method claim.
- ✓ 2. Further, "treatment" for what?
- ✓ 3. "Derivative" formed how? Suggested is "compound" instead in claim 1, line 1.
- ✓ 4. "Substituted" (e.g. tenth from last line of page 72; page 73, R4 definition, etc.) --- with what?

Art Unit: 1624

- ✓ 5. "Heterocyclic" is indefinite. What is the size of the ring? What is the number and nature of the heteroatoms? Can the ring be fused or spiroconnected to another ring, and if so, what kind of ring? Can the ring be bridged? Unsaturated? Cf. *In re Wiggins*, 179 USPQ 421, 423. While it is set forth in some places what this means, in others, e.g. on page 72, it has not been.
- ✓ 6. On page 72, 9th line below the formula there is provided "aliphatic acyl". However, two lines above there is already "aliphatic", which is already embrative of "aliphatic acyl". Thus, it is not clear what role "aliphatic acyl" is supposed to play in the claim, unless the "aliphatic" is not meant to include "aliphatic acyl". If that is so, then what definition of "aliphatic" is being used?
- ✓ 7. Similarly, substituted aliphatic (see page 73, line 4-5) where the substituents are non-cyclic makes no sense. Aliphatic simply means that it lacks cycles, and thus aliphatic already permits those substituents. Thus, it is not clear why such substituents are listed. The same is true for most of the substituents at the bottom of page 76, etc.
- ✓ 8. The role of the "29 C atoms" on page 73 is unclear. Is this the total for the substituent, or just the total in the hydrocarbon part. Thus, would a C₂₉ hydrocarbon substituted by alkoxy be included?
- ✓ 9. The role of the last two terms in the 8th line below the formula on page 72 is unclear. "Carbocyclic-aliphatic" would presumably be something like benzyl. However, that would already be covered by the "carbocyclic" earlier in the line. It may be that applicants intend for "carbocyclic" something which is entirely carbocyclic, and since benzyl is not entirely carbocyclic, then it is not embraced by carbocyclic.

Art Unit: 1624

However, page 79 includes choices like aryl substituted by alkoxy, which is not entirely carbocyclic, and hence that theory is untenable. Clarification is required.

The same problem arises with the R4 definition on page 73.

- ✓ 10. The term "acyl" is indefinite. Does this embrace acids of S? P? As? What does the stem look like, i.e. if the acyl is e.g. RC(O), what is R? In carboxylic acid acyls, does the carbon count include the carbon of the carbonyl?
- ✓ 11. The R5 definition on page 75 is garbled. It never seems to get to what the variable is, and appears repetitive.
- ✓ 12. The term "hydrocarbyl R" on page 76 is mistaken. Most of the R° choices are not hydrocarbyl groups.
- ✓ 13. The term "thio" (last line of page 76) is a generic one, indicating the presence of sulfur in some form. As a substituent, it has no one single generally accepted meaning. There could be intended thioxo (=S) or mercapto (-SH). It can also denote replacement by S of some other atom (normally, oxygen or carbon) as in "thioalkoxy", where O is replaced by S. Perhaps some term which began with "thio", like thiophene was intended. Whatever choice is selected must be supported by the specification.
- ✓ 14. The last term on page 77, line 15 is unclear. Does the 2 refer to the position on the ring or on the ethyl? For whichever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice, and not another, was intended.
- ✓ 15. There is no such thing as "tumor disease". Tumor is a noun, not an adjective.
Deletion of "disease" is suggested.

Art Unit: 1624

- ✓ 16. The moiety bridging sixth and fifth from last line of page 77 is unclear. It starts with a ring being fused, then switches to a substituent, the 6 amino. What is the oxadiazolo fused to?
- ✓ 17. Further, the next two substituents (the last 2 on the list) are unclear. Each have substituents at primed positions (4' and 5'). Where are these? Primed positions are positions not on the central core, but on a side chain. These don't have such side chains.
- ✓ 18. Most of the definitions in the claim 4 R4-R5 combined list that spans pages 77-76 are not permitted choices, and hence claim 5 is improperly dependent on claim 1. These have substituents on the bridge. Thus, for the one bridging the second and last from last line of page 77, there is a $\text{H}_2\text{N}(\text{CH}_2)_2\text{C}(\text{O})$ - attached to the chain. No such substituents are provided for. Its just alkylene or alkenylene (with O, S or N replacing such atoms).
- ✓ 19. The same issue arises with formula II in claim 8. The side chain with R10 is not provided for. A N atom is permitted, not a N atom with another piece on it.
- ✓ 20. In claim 8, line 12, what is that last moiety?
- ✓ 21. Claim 9, line 8 has "radical", which appears in line 4, and thus permits the entire radical (not just R9) to have a substituent. Thus, the substituent could be on the N, surely not what is intended (or described). Likewise claim 10.
- ✓ 22. Certain of the claim 11 species have substituents present with no locant, so it is unknown where the substituent is present. For example, in the first and last species on page 90, the substituent in braces does not have a numeral on it. Thus, this substituent could be on either ring of the biphenyl, or on the N of the amide. For

Art Unit: 1624

whichever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice, and not another, was intended. All species must be checked. On page 94, line 3, what is "the principle of latent functionality"?

✓ 23. Further, what is a "form which can be converted into functional groups"? There is no way to be sure what this does and does not cover.

✓ 24. Claims 20 and 21 are improperly dependent on claim 1, as these intermediates are not provided for by claim 1.

25. Claims 17-18 are incomplete, in that these recite "treatment" but do not say what disorder is being treated. An animal with a tumor disease could in fact have any other disorder.

Claims 17-18 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

See item 25 above. The claim as written embraces treatment of any disorder whatsoever, so long as there is someone with that disorder, plus a tumor or osteoporosis. Thus, this covers treatment of nausea in someone with a tumor, or treatment of a headache in someone with osteoporosis. The specification cannot enable such a panacea, nor does the specification describe this.

Claims 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Even in the event that claim 17 is actually intended to cover just the treatment of tumors, that is also not enabled. The claim would thus set forth the treatment of cancer tumors generally. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

Further, "tumor" covers more than just cancers. It also covers any neoplasm, cancerous or not. A neoplasm is any abnormal tissue that grows by cellular proliferation more rapidly than normal, or continues to grow after the stimulus that initiated the new growth has ceased, or shows lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such a term, and the term "neoplastic cells" covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, and polyps. In addition, it embraces

Art Unit: 1624

various non-cancerous proliferative disorders such as psoriasis, restinosis, vascular smooth muscle proliferation associated with atherosclerosis, glomerular nephritis, clonal proliferative disorders including the various Myelodysplastic Syndromes such as Refractory anemias, certain types of abnormal wound healings, different types of abnormal angiogenesis, pulmonary fibrosis, macular degeneration, myeloproliferative disorders such as primary polycythemia and myleofibrosis, and rheumatoid arthritis.

In addition, "tumor" covers things other than neoplasms. It also covers any kind of swelling arising from inflammation. Thus, the claim would cover treatment of many kinds of inflammation. The specification cannot support that.

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs Novo Nordisk*, 42 USPQ2nd 1001, 1006.

Specification

The abstract has the wrong structure present. It shows an optional bond in the right ring, plural R3 groups (depending on n and m), substitution at the 7-position, etc.

In addition, definition is needed for q and R₁, as that is where the invention lies.

Information Disclosure Statement

The three references which were struck were all incomplete.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

Art Unit: 1624

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.



Mark L. Berch
Primary Examiner
Art Unit 1624

January 25, 2002